

<b>Sanofi</b>	<b>SSR149744C (celivarone)</b>
<b>Mechanism of Action</b>	Anti-arrhythmic, Vaughan Williams Class I to IV
<b>Overview</b>	<p>Celivarone is a benzofuran derivative with a multifactorial mode of action including class IV Vaughan Williams' electrophysiological as well as anti-adrenergic properties. It has no iodine and has a limited tissue accumulation compared with amiodarone. Celivarone exhibits effective anti-arrhythmic properties in several ventricular ischemia- or reperfusion-induced arrhythmia models as well as in <i>in vitro</i> and <i>in vivo</i> atrial fibrillation (AF) models. Its electrophysiological properties are similar to amiodarone (multifactorial mode of action) but with different relative effects on the ion channels. At the ventricular level, celivarone shows anti-arrhythmic activities by suppressing reperfusion-induced arrhythmias (i.v. and oral routes) and reducing the early mortality due to myocardial infarction (oral route) in rats models. At the atrial level, celivarone is effective in atrial fibrillation models with restoration of sinus rhythm or prevention of AF induction and AF recurrence.</p>
<b>Safety/Tolerability</b>	<p>In toxicity studies, celivarone displayed an acceptable safety profile with no unexpected toxicity.</p> <p>Clinical safety was good in healthy subjects across the whole Phase 1 program. Its pro-arrhythmic potential and negative inotropic effect are low and so far, celivarone demonstrated an acceptable safety profile in patients with no evidence of pro-arrhythmia or extra-cardiac toxicities.</p> <p>22 clinical studies have been completed, including a total of 2,167 healthy subjects/patients (of whom approximately 1,600 received celivarone).</p>
<b>Additional Information</b>	The Phase 2 clinical studies did not show the efficacy of celivarone for the prevention of atrial fibrillation/atrial flutter (AF/AFL) nor for the prevention of Ventricular Tachycardia or Ventricular Fibrillation (VT/VF) triggered implantable cardioverter defibrillator (ICD) interventions.
<b>Suitable for and Exclusions</b>	The dosing of the drug is once daily. Celivarone must be taken with food.
<b>Clinical Trials</b>	<a href="http://clinicaltrials.gov/ct2/results?term=SSR149744C+or+celivarone">http://clinicaltrials.gov/ct2/results?term=SSR149744C+or+celivarone</a>
<b>Publications</b>	<a href="http://www.ncbi.nlm.nih.gov/pubmed?term=SSR149744C%20or%20celivarone">http://www.ncbi.nlm.nih.gov/pubmed?term=SSR149744C%20or%20celivarone</a>